



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of	)	
	)	
Jing Wu, et al.	)	Group Art Unit: Unassigned
	)	
Application No.: Unassigned	)	Examiner: Unassigned
	)	
Filed: ON EVEN DATE HEREWITH	)	
	)	
For: CYCLOALKYL, LACTAM, LACTONE	)	
AND RELATED COMPOUNDS,	)	
PHARMACEUTICAL COMPOSITIONS	)	
COMPRISING SAME, AND METHODS	)	
FOR INHIBITING $\beta$ -AMYLOID	)	
PEPTIDE RELEASE AND/OR ITS	)	
SYNTHESIS BY USE OF SUCH	)	
COMPOUNDS	)	

**INFORMATION DISCLOSURE STATEMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. § 1.56, Applicants hereby submit the following information in conformance with 37 C.F.R. §§ 1.97 and 1.98. Pursuant to 37 C.F.R. §1.98, a copy of each of the following documents was submitted in Application No. 08/996,422, upon which is based a claim for priority under 35 U.S.C. §120.

1. U.S. Patent No. 3,657,341, issued April 18, 1972, to Thorne.
2. U.S. Patent No. 4,477,464, issued October 16, 1984, Slade, et al.
3. U.S. Patent No. 4,666,829, issued May 19, 1987, to Glenner, et al.
4. U.S. Patent No. 4,977,168, issued December 11, 1990, to Bernat, et al.
5. U.S. Patent No. 5,238,932, issued August 24, 1993, to Flynn, et al.
6. U.S. Patent No. 5,283,241, issued February 1, 1994, to Bochis, et al.
7. U.S. Patent No. 5,284,841, issued February 8, 1994, to Chu, et al.
8. U.S. Patent No. 5,324,726, issued June 28, 1994, to Bock, et al.
9. U.S. Patent No. 5,360,802, issued November 1, 1994, to Chambers, et al.

10. U.S. Patent No. 5,420,271, issued May 30, 1995, to Warchawsky, et al.
11. U.S. Patent No. 5,556,969, issued September 17, 1996, to Chambers, et al.
12. U.S. Patent No. 5,633,251, issued May 27, 1997, to Claremon, et al.
13. U.S. Patent No. 5,658,901, issued August 19, 1997, to Claremon, et al.
14. U.S. Patent No. 5,712,397, issued January 27, 1998, to Esser, et al.
15. U.S. Patent No. 5,770,573, issued June 23, 1998, to Arrhenius, et al.
16. Canadian Patent No. 1 063 108, published September 25, 1979.
17. European Patent No. 0 167 919, published January 15, 1986.
18. European Patent No. 0 284 256, published September 28, 1988.
19. European Patent No. 0 349 949, published January 10, 1990.
20. European Patent No. 0 376 849, published July 4, 1990. (Abstract in English)
21. European Patent No. 0 434 360, published June 26, 1991.
22. European Patent No. 0 434 364, published June 26, 1991.
23. European Patent No. 0 434 369, published June 26, 1991.
24. European Patent No. 0 490 590, published June 17, 1992.
25. European Patent No. 0 514 133, published November 19, 1992.
26. European Patent No. 0 523 845, published January 20, 1993.
27. European Patent No. 0 549 039, published June 30, 1993.
28. European Patent No. 0 647 632, published April 12, 1995.
29. European Patent No. 0 652 009 A1, published June 10, 1995.
30. European Patent No. 0 667 344, published August 16, 1995.
31. European Patent No. 0 677 517 A1, published October 18, 1995.
32. European Patent No. 0 732 399 A, published September 18, 1996.
33. European Patent No. 0 778 266 A1, published November 6, 1997.
34. GB 1 519 495, published July 6, 1978.
35. GB 1 573 931, published August 18, 1980.
36. GB 2 272 439, published May 18, 1994.
37. GB 2 290 788 A, published January 10, 1996.
38. JP 04210967 A2, published August 3, 1994.
39. JP 06145148 A2, published May 24, 1994.

40. JP 07304770 A2, published November 21, 1995.
41. JP 10072444 A2, published March 17, 1998.
42. International Publication No. WO 92/01683, published February 6, 1992.
43. International Publication No. WO 92/16524, published October 1, 1992.
44. International Publication No. WO 93/19052, published September 30, 1993.
45. International Publication No. WO 93/19063, published September 30, 1993.
46. International Publication No. WO 94/05693, published March 17, 1994.
47. International Publication No. WO 94/04531, published March 3, 1994.
48. International Publication No. WO 94/07486, published April 14, 1994.
49. International Publication No. WO 94/10569, published May 11, 1994.
50. International Publication No. WO 95/03289, published February 2, 1995.
51. International Publication No. WO 95/03290, published February 2, 1995.
52. International Publication No. WO 95/09838, published April 13, 1995.
53. International Publication No. WO 95/14671, published June 1, 1995.
54. International Publication No. WO 95/21840, published August 17, 1995.
55. International Publication No. WO 95/23810, published September 8, 1995.
56. International Publication No. WO 95/25118, published September 21, 1995.
57. International Publication No. WO 95/32191, published November 30, 1995.
58. International Publication No. WO 96/05839, published February 29, 1996.
59. International Publication No. WO 96/16981, published June 6, 1996.
60. International Publication No. WO 96/19492, published June 27, 1996.
61. International Publication No. WO 96/20725, published July 11, 1996.
62. International Publication No. WO 96/22966, published August 1, 1996.
63. International Publication No. WO 96/40146, published December 19, 1996.
64. International Publication No. WO 96/40653, published December 19, 1996.
65. International Publication No. WO 96/40654, published December 19, 1996.
66. International Publication No. WO 96/40655, published December 19, 1996.
67. International Publication No. WO 96/40656, published December 19, 1996.
68. International Publication No. WO 97/30072, published August 21, 1997.
69. International Publication No. WO 97/38705, published October 23, 1997.

70. International Publication No. WO 98/00405, published January 8, 1998.
71. International Publication No. WO 98/25930, published June 18, 1998.
72. International Publication No. WO 98/28268, published July 2, 1998.
73. International Publication No. WO 98/38177, published September 3, 1998.
74. Aquino, et al. "Discovery of 1,5-Benzodiazepines with Peripheral Cholecystokinin (CCK-A) Receptor Agonist Activity. 1. Optimization of the Agonist "Trigger." *J. Med. Chem.* 39: 562-569 (1996).
75. Arienti, et al. "Regioselective Electrophilic Alkylation of Anilines with Phanylacetylene in the Presence of Montmorillonite KSF." *Tetrahedron* 53(10): 3795-3804 (1997).
76. Bock, et al. "Synthesis and Resolution of 3-Amino-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-ones." *J. Org. Chem.* 52: 3232-3239 (1987).
77. Bock, et al. "An Expedient Synthesis of 3-Amino-1,3-Dihydro-5-Phenyl-2H-1,4-Benzodiazepin-2-one." *Tet. Lett.* 28(9): 939-942 (1987).
78. Bock, et al. "Selective Non-Peptide Ligands for an Accommodating Peptide Receptor. Imidazobenzodiazepines as Potent Cholecystokinin Type B Receptor Antagonists." *Bioorg. and Med. Chem. Lett.* 2(9):987-998 (1994).
79. Brown, et al. "A Revision of the structure of "7-Phenyloxindole"; Photochemical Synthesis and Pyrolytic Behaviour of Authentic 7-Phenyloxindole." *Tet. Lett.* 8: 667-670 (1971).
80. Chambers, et al. L-708,474: the C5-Cyclohexyl Analogue of L-365,260, A Selective High Affinity Ligand for the CCKB/Gastrin Receptor." *Bioorg. and Med. Chem. Lett.* 3(10):1919-1924 (1993).
81. Cordell. "B-Amyloid Formation as a Potential Therapeutic Target for Alzheimer's Disease." *Ann. Rev. Pharmacol. Toxicol.* 34:69-89 (1994).
82. Evans, , et al. "Assymetric Synthesis of -Amino Acids, Electrophilic Azidation of Chiral Imide Enolates, a Practical Approach to the Synthesis of (R)- and (S)- Azido Carboxylic Acids." *J. Am. Chem. Soc.* 112: 4011-1030.
83. Evans, et al. "Methods for Drug Discovery: Development of Potent, Selective Orally Effective Cholecystokinin Antagonists." *J. Med. Chem.* 31:2235-2246 (1988).

84. Evans, et al. "Molecular Mimicry and the Design of Peptidomimetics." *Molecular Mimicry in Health and Disease*. (A. Lernmark, et al., eds.) Elsevier Science Publishers B.v. (Biomedical Division) (1988) pp. 23-34.
85. Finizia, et al. "Synthesis and Evaluation of Novel 1,5-Benzodiazepines as potent and selective CCK-B Ligands, Effect of the Substitution of the N-5 Phenyl with Alkyl Groups." *Bioorg. & Medicinal Chemistry Letters*. 6(24):2957-2962 (1996).
86. Hirst, et al. "Discovery of 1,5-Benzodiazepines with Peripheral Cholecystokinin (CCK-A) Receptor Agonists Activity (II): Optimization of the C3 Amino Substituent." *J. Med. Chem.* 39: 5236-5245 (1996).
87. Hofmann, et al. "Interactions of Benzodiazepine Derivatives with Annexins." *J. Biol. Chem.* 273(5):2885-2894 (1998).
88. Katrizky, et al. "Benzodiazepine Derivatives with Annexins." *J. Biol. Chem.* 273(5): 2885-2894 (1998).
89. Lowe, et al. "A Water Soluble Benzazepine Cholecystokinin-B-Receptor Antagonist." *Bioorg. and Med. Chem. Lets.* 5(17): 1933-1936 (1995).
90. Lowe, et al. "5-Phenyl-3-ureidobenzazepin-2-ones as Cholecystokinin-B Receptor Antagonists." *J. Med. Chem.* 37: 3789-3811 (1994).
91. Milligan, et al. "Intramolecular Schmidt Reactions of Alkyl Azides with Ketones: Scope and Stereochemical Studies." *J. Am. Chem. Soc.* 117: 10449-10459 (1995).
92. Papadopoulos, et al. "Anodic Oxidation of N-Acyl and N-Alkoxy carbonyl Dipeptide Esters as a Key Step for the Formation of Chiral Heterocyclic Synthetic Building Blocks." *Tetrahedron* 47(4/5):563-572 (1991).
93. Patel, et al. "Biological Properties of the Benzodiazepine Amidine Derivative L-740,093, a Cholecystokinin-B/Gastrin Receptor Antagonist with High Affinity in vitro and High Potency in vivo." *Molecular Pharmacology*. 46:943-948 (1994).
94. Reiter, et al. "Crystallization-Induced Asymmetric Transformation: Stereospecific Synthesis of a Potent Peripheral CCK Antagonist." *J. Org. Chem.* 52: 955-957 (1987).
95. Rittle, et al. "A New Amine Resolution Method and its Application to 3-Aminobenzodiazepines." *Tet. Lets.* 28(5):521-522 (1987).
96. Robl. "Synthesis of 2-(4-Fluorophenyl)-4-isopropyl-3-quinolinecarbaldehyde: A New Route to 2,3,4-Substituted Quinolines." *Synthesis*. 56-58 (1991).

97. Satoh, et al. "New 1,4-Benzodiazepine-2-one Derivatives as Gastrin/Cholecystokinin-B Antagonists." *Chem. Pharm. Bull.* 43(12): 2159-2167 (1995).
98. Satyanarayana, et al. "Carbonylation of Benzyl Halides Using CoCl<sub>2</sub>/NaBH<sub>4</sub>/CO/NaOH Reagent System." *Tet. Lets.* 28(23): 2633-2636 (1987).
99. Semple, et al. "Design, Synthesis, and Evolution of a Novel, Selective, and Orally Bioavailable Class of Thrombin Inhibitors: P1-Argininal Derivatives Incorporating P3-P4 Lactam Sulfoamide Moieties." *J. Med. Chem.* 39: 4531-4536 (1996).
100. Sherrill, et al. "An Improved Synthesis and Resolution of 3-Amino-1,3 dihydro-5-phenyl-2H-1,4-benzodiazepinn-2-ones." *J. Org. Chem.* 60:730-734 (1995).
101. Showell, et al. "High Affinity and Potent, Water-Soluble 5-Amino-1,4-Benzodiazepine CCKB/Gastrin Receptor Antagonists Containing a Cationic Solubilizing Group." *J. Med. Chem.* 37:719-721 (1994).
102. Smith, et al. "β-APP Processing as a Therapeutic Target for Alzheimer's Disease." *Current Pharmaceutical Design.* 3:439-445 (1997).
103. Stewart. "Syntheses of L-Kynurenine Peptides Conducted Without Masking the Side-Chain Amino Group." *Aust. J. Chem.* 33: 633-640 (1980).
104. Van Niel, et al. "CCKB Selective Receptor Ligands: Novel 1,3,5-Trisubstituted Benzazepin-2-ones." *Bioorganic & Medicinal Chemistry Letters.* 5(13):1421-1426 (1995).
105. Varnavas, et al. "Synthesis of New Benzodiazepine Derivatives as Potential Cholecystokinin Antagonists." *Il Farmaco.* 46(2):391-401 (1991).
106. Waldmann, et al. "Selective Enzymatic Removal of Protecting Groups: The Phenylacetamide as Amino Protecting Group in Phosphopeptide Synthesis." *Tet. Lets.* 37(48): 8725-8728 (1996).
107. Warshawsky, et al. "The Synthesis of Aminobenzazepinones as Anti-Phenylalanine Dipeptide Mimics and Their Use in NEP Inhibition." *Bioorg. & Med. Chem. Lets.* 6(8): 957-962 (1996).
108. Zoller, et al. "Aminoalkylation of Cercaptans with Glyoxylic Acid Derivatives." *Tetrahedron.* 31: 863-866 (1973).

The documents are being submitted before the first Office Action on the merits, therefore no fee or certification is required under 37 C.F.R. § 1.97(b). In the event that an Office Action is mailed prior to receipt of this paper, the Commissioner is hereby authorized to charge the requisite fees under 37 C.F.R. § 1.97(c) for submission of this paper to Deposit Account No. 02-4800.

By citing the above references, Applicants do not acquiesce or admit that any of these documents are "prior art" under 35 U.S.C. Applicants specifically reserve the right, where appropriate, to antedate any of the cited documents by an appropriate showing under 37 C.F.R. § 1.131, § 1.604, § 1.608 or any other suitable means.

To assist the Examiner, the documents are listed on the attached form PTO-1449. It is respectfully requested that an Examiner initialed copy of this form be returned to the undersigned.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Lawrence S. Squires  
Lawrence S. Squires  
Registration No. 24,060

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(650)622-2300

Date: July 26, 2001